

### R E M A R K S

Claims 1 and 7 were amended by including the feature of claims 4 and 10.

Claims 5, 11 and 15 were amended to change the dependency of such claims, in view of the cancellation of claims 4 and 10.

Enclosed is a MARKED-UP VERSION OF THE AMENDMENTS TO THE CLAIMS.

With respect of Rule 116, entry of the above amendments is respectfully requested, since the amendments to the claims involve a feature that was included in th claims prior to the Final Rejection.

Claims 1 and 3 were rejected under 35 USC 102 as being anticipated by JP 9020660 for the reasons set forth at the bottom of page 2 of the Office Action.

Claims 1, 3, 6, 7, 9, 12, 14 and 18 were rejected under 35 USC 102 as being anticipated by Nagrisoli EP 449787 for the reasons set forth at the top of page 3 of the Office Action.

There were no anticipation rejections for claims 4, 5, 10, 11, 13, 15 to 17 and 19.

In view of the incorporation of the feature of claims 4 and 10 into claims 1 and 7, it is respectfully submitted that the anticipation rejections are moot. Withdrawal of the anticipation rejections is therefore respectfully solicited.

Claims 17 and 19 were rejected under 35 USC 103 as being unpatentable over Nagrisoli EP 449787 for the reasons set forth at the bottom of page 3 of the Office Action.

Claims 4 to 5, 9 to 11, 13 and 15 to 16 were rejected under 35 USC 103 as being unpatentable over Nagrisoli in view of EP 652012 for the reasons set forth on page 4 of the Office Action.

Nagrisoli describes that any one of amino acids, sugars, mineral salts and vitamins may be incorporated as other active ingredients in combination with a dipeptide. However, with respect to the sugar, only glucose is specifically indicated in Example 1 at the bottom of page 2 of EP 449787.

In Example 25 on page 7, column 12 of EP 652012, a composition for treatment of chronic fatigue syndrome is described. However, EP 652012 does not provide any data showing the effects of treatment of chronic fatigue syndrome.

Further, the muscular fatigue described in Nagrisoli and the chronic fatigue syndrome described in EP 652012 are fundamentally different in the respective causes and symptoms. A drug useful for chronic fatigue is not necessarily useful for muscular fatigue. Accordingly, it is respectfully submitted that one of ordinary skill in the art would not consider that the composition for chronic fatigue syndrome described in EP 652012 would be appropriate to enhance the treatment of muscular fatigue described in Nagrisoli.

Moreover, EP 652012 discloses a composition for treatment of diseases of the brain, such as drug-dependence, drunkenness, Alzheimer's disease and schizophrenia, as described on page 1, column 1, lines 20 to 22 of EP 652012. The uses of the composition described in EP 652012 include hair growth, application to drunkenness and other research and treatment

applications, as described in Example 1 on pages 4 to 5 of EP 652012. With respect to the effects for recovery from fatigue, only the words "treatment of chronic fatigue syndrome" are indicated in Example 25 of EP 652012.

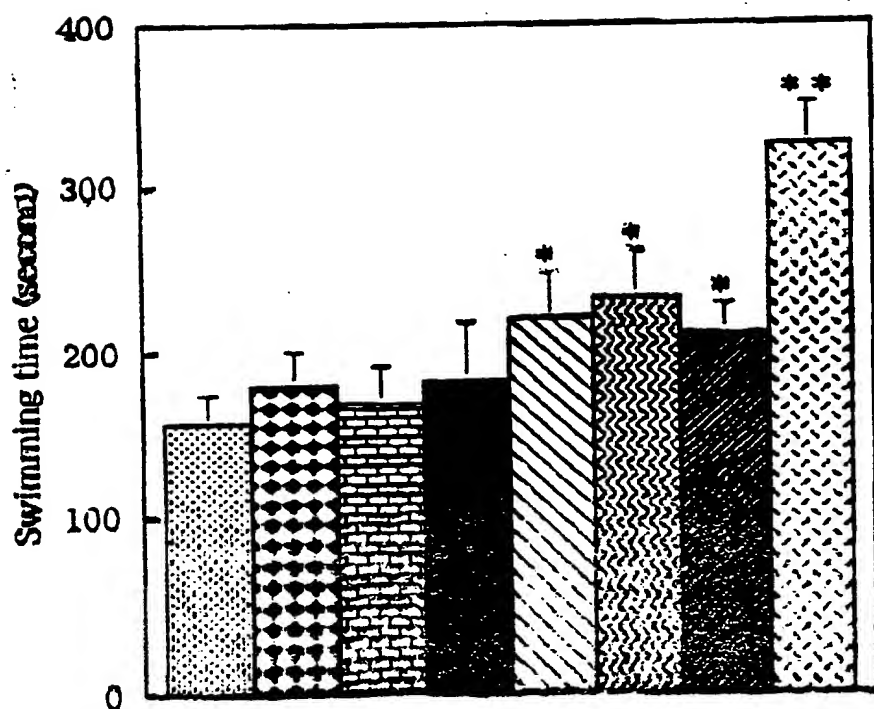
Namely, it is respectfully submitted that one of ordinary skill in the art would not have sufficient information from EP 652012 to apply the active ingredient of EP 652012, which was basically developed for treatment of symptoms of the brain, to the composition of Nagrisoli, which was developed for treatment of muscular fatigue.

Still further, the active ingredient of Nagrisoli is carnosine, homocarnosine, anserine, homoanserine, ophidine or physiologically equivalent derivatives thereof. With respect to sugar, Nagrisoli disclose only that the sugar may be incorporated as another component and, specifically, as discussed above, in Nagrisoli only glucose is disclosed. Moreover, "ribose" is only one of several types of sugars described in EP 652012. Accordingly, it is respectfully submitted that one of ordinary skill in the art would not easily choose "ribose" as the sugar to employ in view of the several types of sugars described in EP 652012.

Submitted concomitantly herewith is a DECLARATION UNDER 37 CFR 1.132 of Yoshiharu MATAHIRA (unexecuted; an executed version of the DECLARATION UNDER 37 CFR 1.132 will be submitted shortly).

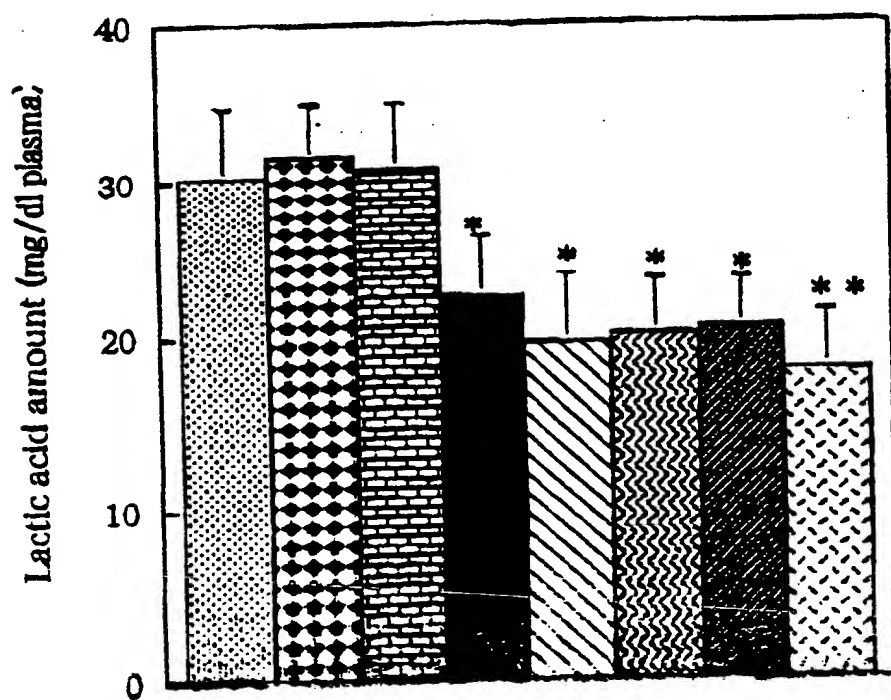
The results of the enclosed MATAHIRA DECLARATION are summarized in Figs. 1 and 2 therein, which are reproduced as follows:

Fig. 1



- Control Group
- Glucose-administrated group
- Fructose-administrated group
- Ribose-administrated group
- Anserine-administrated group
- Anserine/Glucose mixture-administrated group
- Anserine/Fructose mixture-administrated group
- Anserine/Ribose mixture-administrated group

Fig. 2



- \* showed significant difference ( $p < 0.05$ ) as compared with the control group
- \*\* showed significant difference ( $p < 0.01$ ) as compared with the control group

As is evident from the results of the experiments set forth in the enclosed MATAHIRA DECLARATION, that the anserine/ribose mixture administration group showed a significantly prolonged swimming time as compared with the anserine administration group, the glucose administration group, the fructose administration group, the ribose administration group, the anserine/glucose mixture administration group and the anserine/fructose mixture administration group (see Fig. 1). Further, the anserine/ribose mixture administration group showed the lowest lactic acid amount in the plasma after the loading of exercise (see Fig. 2).

The results of the MATAHIRA DECLARATION thus establish expected results for the combined use of anserine and D-ribose in accordance with the presently claimed invention.

With respect of Rule 116, consideration of the MATAHIRA DECLARATION is respectfully requested, since the MATAHIRA DECLARATION serves to reply to rejections involving references that were cited for the first time in the Final Rejection.

It is therefore respectfully submitted that applicants' claimed invention is not anticipated and is not rendered obvious by the references.

Reconsideration is requested. Allowance is solicited.

A REQUEST FOR ACKNOWLEDGMENT OF RECEIPT OF CERTIFIED COPIES OF PRIORITY DOCUMENTS is submitted herewith.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



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- Encs.: (1) PETITION FOR EXTENSION
- (2) MARKED-UP VERSION OF THE AMENDMENTS TO THE CLAIMS
- (3) Unexecuted DECLARATION UNDER 37 CFR 1.132 of Yoshiharu MATAHIRA
- (4) REQUEST FOR ACKNOWLEDGMENT OF RECEIPT OF CERTIFIED COPIES OF PRIORITY DOCUMENTS



MARKED-UP VERSION OF THE AMENDMENTS TO THE CLAIMS  
(U.S. SERIAL NO. 09/933,438)

1. (Thrice Amended) An antifatigue composition which comprises an antifatigue effective amount of (a) at least one imidazole compound selected from the group consisting of anserine, carnosine [and], valenine[, ] and salts thereof, and (b) D-ribose, as [an] active [ingredient] ingredients, in combination with an excipient.

5. (Amended) The antifatigue composition according to Claim [4] 1, wherein the imidazole compound is contained in an amount of from 5 to 50 mass % and the D-ribose is contained in an amount of from 5 to 50 mass %.

7. (Twice Amended) A method for providing an antifatigue effect comprising orally administering to a person in need thereof an antifatigue effective amount of an antifatigue composition which comprises [an antifatigue effective amount of] (a) at least one imidazole compound selected from the group consisting of anserine, carnosine, valenine and salts thereof, [an] and (b) D-ribose, as [an] active [ingredient] ingredients.

11. (Amended) The method according to Claim [10] 7, wherein the imidazole compound is contained in an amount of from 5 to 50

mass % and the D-ribose is contained in an amount of from 5 to 50 mass %.

15. (Amended) The method according to Claim [10] 7, wherein the imidazole compound and the D-ribose are administered in a total daily dosage of 1 to 200 mg/kg of body weight.